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A Review on Current Scenario of Rheumatoid Arthritis in Health Care Practice

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A B S T R A C T

It is a chronic inflammatory disorder of joints affects the diarthrodial joints and especially in the fingers, wrists, feet, and ankles. It is known as autoimmune disorder because it affects the immune system. The disease affects fourth and sixth decade of the life. The genetics, infections, vitamin-D deficiency in the bones, smoking has a significant role in progression of the disease. It is a systemic disorder affects the body. The B cells, T cells MHC cells activated when the immune system is days regulated. The symptoms include morning stiffness, rheumatoid nodules formation, systemic arthritis, pain in the fingers, wrists, feet, and ankles extra articular lesions formation cardio myopathy, bone marrow depression, pleural effusion. The diagnosis of the disease includes the presence of rheumatoid factor in the blood. Elevated Erythrocyte sedimentation rate, C reactive proteins rate, blood test, X rays of hand reveals the disease progression. The management of disease includes disease modifying Anti Rheumatoid Drugs, Interleukin antagonist, anti TNF agents, Non-steroidal anti-inflammatory drugs.

Keywords: Arthritis, Disease, Genetics, Immune System.

A R T I C L E I N F O

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1. Introduction

It is autoimmune disorder that primarily affects joints. It produces warmness, swelling, and pain in the joints [1].The disease affects the other parts of the body. The changes in low red blood cells, inflammation around the lungs,

and inflammation around the heart. Fever and low energy may also be present. Rheumatoid arthritis (RA) is a chronic disease in which all the joints in the body are inflamed, leading to swelling, pain, stiffness, and loss of function. The symptoms are prolongs from weeks to months. It is a chronic systemic inflammatory disease of unknown cause. Rheumatoid arthritis is an autoimmune disease in which the body's immune system attacks joints and other tissues. The pattern of joints affected is usually involves the hands and other joints, and pain in the morning. Rheumatoid arthritis is a systemic (body-wide) disease, involving other body organs.

The disease process begins in the *synovium* the membrane that surrounds a joint and creates a protective sac. This sac is filled with lubricating fluid known as synovial fluid. In addition to cushioning joints, this fluid supplies nutrients and oxygen to cartilage, a slippery tissue that coats the ends of bones. Cartilage is composed of collagen, is the structural protein in the body, which forms a mesh like structure it give support and protection and flexibility to the joints [2].

The inflammation of the synovium. Collagen is gradually destroyed, narrowing the joint space and damaging bone. The pannus produces more enzymes that destroy nearby cartilage, aggravates the area and attracting more inflammatory white cells, thereby perpetuating the process. This inflammatory process not only affects cartilage and bones but can also harm organs in other parts of the body.

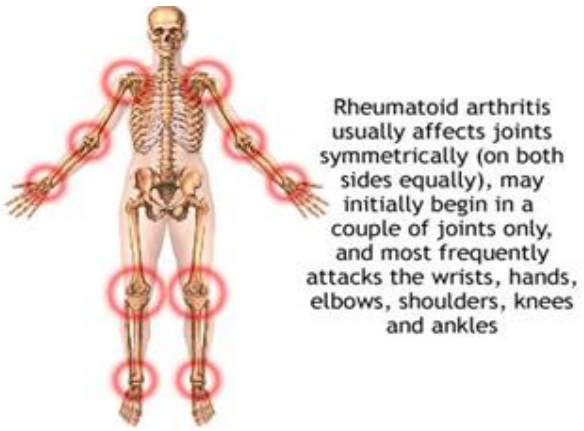


Figure 1: Rheumatoid Arthritis

Etiology: Genetics, smoking, alcohol, infections, vitamin D deficiency in the bones, Hyper prolactinemia.

Risk Factors

- **Age:** onset begins between the ages of 30 - 50 years.
- **Gender:** Women are more likely to develop RA than men.
- **Family History:** Some people may inherit genes that make them more susceptible to developing RA
- Smoking [3]

Complications of Rheumatoid Arthritis

- joint Deterioration and Pain
- Peripheral Neuropathy
- Anemia
- Ocular problems
- Infections
- Skin Problems
- Osteoporosis
- Lung Disease
- Vasculitis
- Heart Disease
- Cancers
- Periodontal Disease
- Kidney and Liver Problems
- Pregnancy Complications

Epidemiology

Worldwide, the annual incidence of RA is approximately 3 cases per 10,000 population, and the prevalence rate is approximately 1%, increasing with age and peaking between the ages of 35 and 50 years. The affecting significance of individuals with RA are at 2- to 3-folds higher risk for the disease [4]. Disease concordance with monozygotic twins is approximately 15-20%. Women are affected by RA approximately 3 times more often than men. It affects 0.3% to 2.3% of the population.

2. Pathophysiology

- Synovial cell hyperplasia and endothelial cell activation are early events in the pathologic process that progresses to uncontrolled inflammation and consequent cartilage and bone destruction [4].
- The Genetic factors and immune system abnormalities contributes to disease propagation. The immune system dys-regulated by entry of pathogenic substances in the body.
- The antigens reacts with anti bodies to form ag-Ab complexes.
- The activation of CD4 T cells, B cells, cytokines [5] plays a major role in the prevention of the inflammatory responses in the body.
- The B cells produce antibodies against the inflammation [6].
- Abnormal production of numerous cytokines, chemokines, and other inflammatory mediators (e.g. tumor necrosis factor alpha [TNF-a], interleukin [IL]-1, IL-6, IL-8, transforming growth factor beta [TGF-ß], fibroblast growth factor [FGF], and platelet-derived growth factor [PDGF])
- It causes the inflammation and proliferation of the synovium. (i.e. pannus)
- It leads to destruction of various tissues, including cartilage (see the image below), bone, tendons, ligaments, and blood vessels by the secretion of collagenase, elastagen, and bone matrix destruction enzymes in the bone marrow.
- The increase secretion of antibodies that forms the auto anti body complexes in the bone matrix and produce the inflammation, destruction of the joints.

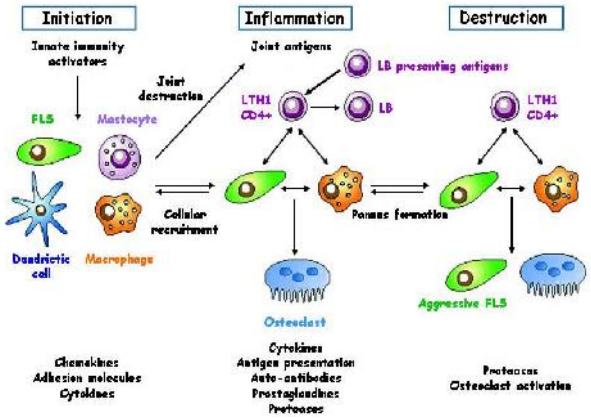
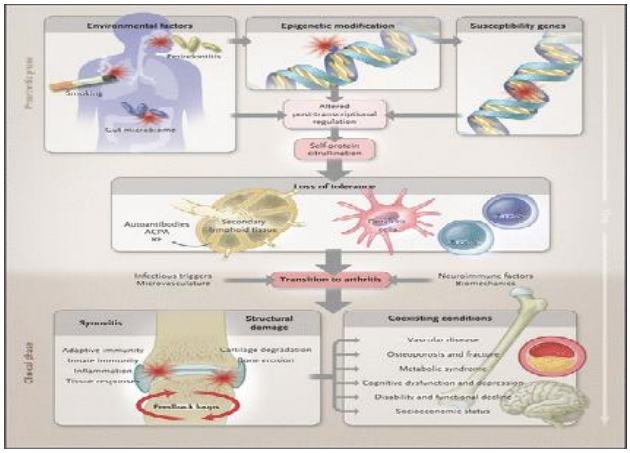


Figure 2: Pathophysiology of Rheumatoid Arthritis



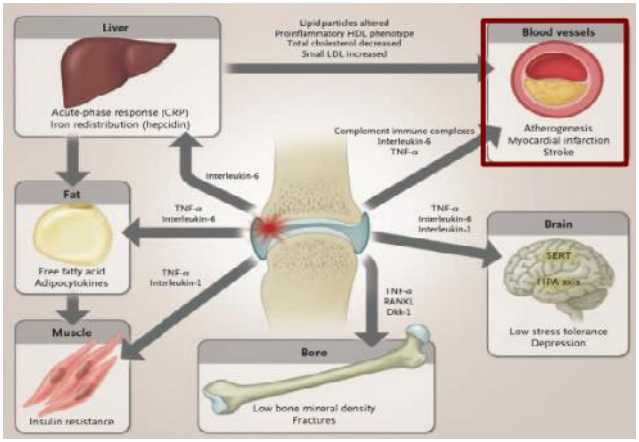


Figure 2: Mechanisms in Rheumatoid Arthritis

3. Clinical Presentation

- Morning stiffness of near joints
- Arthritis in soft tissue swelling, including right or left PIP, MCP, wrist, elbow, MTP, ankle, or knee joints. Rheumatoid nodules, plueral effusions, plueral erosions.
- Malaise, fatigue, weight loss, fever
- Severe motion impairment in radiologic evidence of bone damage.
- Rheumatoid nodules, vasculitis, hematologic abnormalities,
- Bone marrow depression
- Lymph adenopathy
- Symmetrical arthritis in the areas noted in criteria in PIP, MCP, and MTP
- Breathing related problems
- Cardiomyopathy [7]

Diagnosis

The elevated levels of Erythrocyte sedimentation rate and C-reactive proteins. The radiographic features of the hand joints in early disease are characterized by soft tissue swelling and mild juxta-articular osteoporosis [8]. The magnetic resonance, computed tomography and scintigraphy may provide useful information about the features and the extent for anatomical damage in rheumatoid arthritis patients [9].

Treatment: Pharmacotherapy

Table 1: Disease-Modifying Anti-rheumatic Drugs (DMARDS)

Drug	Dose
Methotrexate	7.5-15mg/once weekly
Hydro chloroquine	500 mg od
leflunomide	100 mg od
sulfasalizine	500 mg od

Mechanism of action of methotrexate

This metabolite inhibits B- and T-cell proliferation, antibody secretion, and cellular adhesion. Leflunomide's active metabolite inhibits nucleotide (pyrimidine) synthesis through inhibition of dihydro-orotate dehydrogenase.

Adverse effects

Hepatic effects, nausea and/or vomiting, gastrointestinal effects, leukopenia.

Table 2: Tumor Necrosis Factor-α Inhibitors

Drug	Dose
Adalimumab	30 mg/once weekly
etarncept	40 mg/once weekly
infliximumab	3 mg/once weekly

Mechanism of action

These agents bind TNF-α and then removed by phagocytic cells, leading to a decrease in TNF-α concentrations, binding to receptors, and subsequent actions. TNF-α blockade causes the decreases neutrophil migration into inflamed joints site and diminishes the secretion of IL-1, IL-6, and IL-8, and inhibits cartilage destruction [10].

Table 3: Interleukin-1 Inhibitors

Drug	Dose
Rituximumab	30mg
Anakinra	40mg

Mechanism of action: IL-1 blockade blocks macrophage infiltration in the synovium in patients and inhibits cartilage destruction.

Table 4: Calcineuron Inhibitors

Drug	Dose
Cyclosporine	1.5 g od
cyclophosphamide	1 g od

Mechanism of action:
These cells causes the inhibit calcineurin and inhibits the bone matrix destruction.
Adverse effects: Nephrotoxicity, hypertension, infection, gingival hyperplasia, hypertrichosis, fatigue, and gastrointestinal and neurologic
Drug interactions: Drugs that enhance (e.g., rifampin, phenytoin) or inhibit (e.g., cimetidine, ketoconazole, ciprofloxacin) CYP3A4 will alter the clearance of cyclosporine. Drugs with renal toxicity may also enhance the renal toxicity of cyclosporine.
Major adverse effects
Major adverse effects include gastrointestinal disturbances, weight loss, allergic reactions, transient elevations of liver transaminases, and reversible alopecia [11].
Azathioprine: 1.0 to 2.5 mg/kg/day, or 50 to 200 mg per day. Azathioprine has a half-life of 0.2 to 1 hour,
Mechanism of azathoprine
Purine inhibition by 6-mercaptopurine inhibits proliferation of lymphocytes and other white blood cells
Adverse effects
1. Severe bone marrow
2. Mycophenolate Mofetil: doses of 1-3 mg per day.
Mechanism: reversible inhibitor of inosine monophosphate dehydrogenase that disrupts the synthesis of guanine nucleotides [12]. MMF appears to inhibit the proliferation of lymphocytes to a greater extent than the proliferation of other cells.
Adverse Effects: Nausea, vomiting, abdominal pain, and diarrhea, are the most common adverse effects. However, bone marrow suppression and liver toxicity have been reported in transplant patients.
Sulfasalazine: Adverse Effect: it includes nausea and/or vomiting, skin rash, liver effects leukopenia, fever, anemia and lung effects
Antimalarials: Hydroxychloroquine is used at doses of 2 to 4 mg per kg or 200 to 400 mg per day orally. [13]
Adverse effects
It includes gastrointestinal tract effects (4.6%), rash (2.3%), ocular problems (0.7%), and, less commonly, leukopenia and central nervous system, neuromuscular, and cardiac effects [14], allergic rashes, hemolytic anemia, and gastrointestinal and neurologic effects.
Nonsteroidal Anti-Inflammatory Drugs
NSAIDs inhibit prostaglandins synthesis and inhibition of cyclooxygenase-enzyme results in inhibits the inflammation.

Table 4: Nonsteroidal Anti-Inflammatory Drugs

Drug	Dose
Diclofenac	150–200 mg od
Etodolac	800–1,200 mg od
Indomethacin	150 mg od
Piroxicam	10-20 mg od
Sulindac	300-400 mg od
Fenoprofen	200-300 mg od
Flurbiprofen	200-300 mg od
Celecoxib	200-400 mg od
Ibuprofen	100 mg od
Valdecoxib	200 mg od

Adverse effects
Gastrointestinal effects, the most common problem associated with NSAIDs, include discomfort, distress, nausea, vomiting, diarrhea, bleeding, and ulceration [15].
Drug interactions of NSAIDS
(β-blockers, ACE inhibitors) and loop diuretics, (e.g., warfarin, diazepam).
Corticosteroids
Mechanism of action:
Corticosteroids inhibit T- and B-cell activity and chemotaxis, migration of leukocytes, A dose of 2.5 to 10 mg of Prednisolone methyl prednisolone (1 g daily intravenously for 1 to 3 days). Adverse effects include hyperglycemia, immuno-suppression, sodium and fluid retention, hypotension, and the rare occurrence of seizures, cardiac arrhythmias, sudden death, and gastrointestinal ulceration. [16]
Non Pharmacologic Therapy For The Management Of Rheumatoid Arthritis

- Emotional support to the patient
- Rest and exercise
- Occupational therapy
- Vitamin E supplementation [17] (α-tocopherol 1,200 mg/day)

Improving Outcomes

- Patient Education
- self-awareness,
- Self-determination, and self-reliance, as well as the knowledge of when to seek help from others. Family support is essential [19], especially because of negative attitudes toward the patient's disease that may leads to less coping the disease.

4. Conclusion

The rapid assessment of Rheumatoid arthritis leads to minimize the further complications of the disease. The newer developments in the management of rheumatoid arthritis have made significant approaches to reducing the disease progression and improving outcomes of the patients. The use of biological agents to reduce the disease complications can results in recovery and improving quality of life in patients of rheumatoid arthritis. With the use of medications regular interventions with the patient. Initial diagnosis of the disease and controlling the risk factors exposure we can prevent the disease progression [20].

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